CLAIM SUMMARY DOCUMENT:

Claim 1. (Previously Presented) A method of encapsulating an active substance in a biodegradable polymer, which comprises:

a) dissolving said biodegradable polymer in an organic solvent therefor;

b) dispersing said active substance in the organic solution obtained in step a), to provide a dispersion with the active substance as the inner phase thereof; and

c) subjecting the dispersion obtained in step (b), to an encapsulation operation with an aqueous polyethylene glycol solution as a continuous phase, such that micro- or nanoparticles having the active substance encapsulated therein are obtained;

wherein the biodegradable polymer is homo- or copolymers prepared from α-hydroxy acids or cyclic dimers of α-hydroxy acids or a combination thereof

~~wherein the biodegradable polymer can only be dissolved in an organic solvent~~.

Claim 2. (Currently Amended) A method according to claim 1, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 20-80% (w/w)~~, preferably 20-60% (w/w), such as 30-55% (w/w) or 30-50% (w/w)~~.

Claim 3. (Currently Amended) A method according to claim 1, wherein the polyethylene glycol has a molecular weight of about 1000 to 40000 Da~~, preferably about 5000 to 35000 Da~~.

Claim 4. (Previously Presented) A method according to claim 1, wherein the encapsulation operation in step c) is performed by adding the dispersion obtained in step b), to said aqueous polyethylene glycol solution while subjection last-mentioned aqueous solution to a stirring and homogenization operation.

Claim 5. (Previously Presented) A method according to claim 4, wherein the stirring and homogenization operation is performed by a low intensity and low energy process, e.g., propeller mixing or the use of motionless mixers.

Claim 6. (Previously Presented) A method according to claim 1, wherein said encapsulation operation in step c) is performed in the absence of any surfactant.

Claim 7. (Currently Amended) A method according to claim 1, wherein said biodegradable polymer is insoluble in the aqueous polyethylene glycol solution used in step c)~~, preferably an aliphatic polyester~~.

Claim 8. (Currently Amended) A method according to claim 1, wherein said biodegradable polymer has a weight average molecular weight in the range of about 2000 to 200 000~~, preferable about 2000 to 110 000~~.

Claim 9. (Canceled)

Claim 10. (Currently Amended) A method according to claim 1 9, wherein a copolymer of lactic acid/glycolic acid or a mixture of polylactic acid/polyglycolic acid is used as said biodegradable polymer, the weight ratio of (poly)lactic acid/(poly)glycolic acid being within the range of about 99/1 to 35/65~~, preferably 95/5 to 50/50~~.

E1 cont'd

Claim 11. (Currently Amended) A method according to claim 1, wherein said organic solvent used in step a) is immiscible or essentially immiscible with said aqueous polyethylene glycol solution used in step c), but slightly or very slightly soluble therein, and capable of dissolving said biodegradable polymer~~, and is preferably selected from ethyl acetate, dichloromethane, methyl ethyl ketone and methyl isobutyl ketone~~.

Claim 12. (Currently Amended) A method according to claim 1, wherein the active substance which is dispersed in step b) has a particle size within the range of about 0.5-20 μm~~, preferably 0.5-10 μm, more preferably 0.5-3 μm~~.

Claim 13. (Previously Presented) A method according to claim 1, wherein said active substance is a biologically active substance~~, which is preferably selected from proteins, (poly)peptides, (poly)nucleotides, plasmides and DNA~~.

Claim 14. (Currently Amended) A method according to claim 13, wherein said biologically active substance is selected from the group consisting of growth hormone, erythropoictin, interferon (α, β, γ-type), vaccine, epidermal growth hormone, Factor VIII, LHRH analogue, inulin, macrophage colony stimulating factor, granulocyte colony stimulating factor and interleukin.

E1 cont'd

Claim 15. Currently Amended) A method according to claim 1, wherein said active substance is a biologically active substance in the form of a non-protein drug selected from the group consisting of ~~from the following groups:~~ anti-tumor agents, antibiotics, anti-flammatory agents, antihistamines, sedatives, muscle relaxants, antiepileptic agents, antidepressants, antiallergic agents, bronchodilators, cardiotonics, antiarrythmic agents, vasodilators, antidiabetic agents, anticoagulants, hemostatics, narcotic agents and steroids.

Claim 16. (Currently Amended) A method according to claim 1, wherein said active substance is a non-biological substance~~, which is preferably selected from pesticide, fragrance, flavouring agent, catalyst and herbicide~~.

Claim 17. (Currently Amended) A method according to claim 1, wherein the amount of said active substance is in the range of about 0.001% to 90%~~, preferably about 0.01% to 70%, more preferably about 0.1 to 45%, and most preferably about 0.1 to 40%~~, said percentage being by weight based on the weight of the final particles.

Claim 18. (Currently Amended) A method according to claim 1, wherein the particles obtained in step c) are separated from said continuous phase~~, preferably by centrifugation or filtration followed by rinsing with water or other aqueous medium~~, and dried or allowed to dry, for instance in a vacuum, in the presence of a nitrogen gas flow, by lyophilisation or by air suspension drying.

E1 cont'd

Claim 19. (Previously Presented) A method according to claim 1, wherein step c) is performed such that the particles obtained are microspheres or capsules or nanospheres or capsules.

Claim 20. (Original) A method according to claim 19, wherein said particles have a mean diameter in the range of 10-200 μm, preferably 10-100 μm.

Claim 21. (Previously Presented) Sustained release micro or nanoparticles containing an active substance encapsulated in a biodegradable polymer, obtainable by the method of claim 1.

Claim 22. (Original) Particles according to claim 21, which are suitable for parenteral, nasal, pulmonal or oral administration of said active substance.

Claim 23. (Currently Amended) A method according to claim 1, wherein said biodegradable polymer is slightly soluble in the aqueous polyethylene glycol solution used in step c)~~, preferably an aliphatic polyester~~.

Claim 24. (Currently Amended) A method of encapsulating an active substance in a biodegradable polymer, which comprises:

a) dissolving said biodegradable polymer in an organic solvent therefor;

b) emulsifying said active substance, dissolved in water or other aqueous solvent therefor, in the organic solution obtained in step a), to provide an emulsion with the active substance as the inner aqueous phase thereof; and

c) subjecting the dispersion obtained in step b) to an encapsulation operation with an aqueous polyethylene glycol solution as a continuous phase, such that micro- or nanoparticles having the active substance encapsulated therein are obtained;

wherein the biodegradable polymer is homo- or copolymers prepared from α-hydroxy acids or cyclic dimers of α-hydroxy acids or a combination thereof

~~wherein the biodegradable polymer can only be dissolved in an organic solvent~~.

Claim 25. (Currently Amended) A method according to claim 1, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 20-80% (w/w)~~, preferably 20-60% (w/w), such as 30-55% (w/w) or 30-50% (w/w)~~.

Claim 26. (Currently Amended) A method according to claim 1, wherein the polyethylene glycol has a molecular weight of about 1000 to 40000 Da~~, preferably about 5000 to 35000 Da~~.

Claim 27. (Previously Presented) A method according to claim 1, wherein the encapsulation operation in step c) is performed by adding the dispersion obtained in step b) to said aqueous polyethylene glycol solution while subjection last-mentioned aqueous solution to a stirring and homogenization operation.

Claim 28. (Previously Presented) A method according to claim 4, wherein the stirring and homogenization operation is performed by a low intensity and low energy process, e.g., propeller mixing or the use of motionless mixers.

Claim 29. (Previously Presented) A method according to claim 1, wherein said encapsulation operation in step c) is performed in the absence of any surfactant.

Claim 30. (Currently Amended) A method according to claim 1, wherein said biodegradable polymer is insoluble in the aqueous polyethylene glycol solution used in step c)~~, preferably an aliphatic polyester~~.

Claim 31. (Currently Amended) A method according to claim 1, wherein said biodegradable polymer has a weight average molecular weight in the range of about 2000 to 200,000~~, preferable about 2000 to 110,000~~.

Claim 32. (Canceled)

Claim 33. (Currently Amended) A method according to claim 1 9, wherein a copolymer of lactic acid/glycolic acid or a mixture of polylactic acid/polyglycolic acid is used as said biodegradable polymer, the weight ratio of (poly)lactic acid/(poly)glycolic acid being within the range of about 99/1 to 35/65, preferably 95/5 to 50/50.

Claim 34. (Currently Amended) A method according to claim 1, wherein said organic solvent used in step a) is immiscible or essentially immiscible with said aqueous polyethylene glycol solution used in step c), but slightly or very slightly soluble therein, and capable of dissolving said biodegradable polymer~~, and is preferably selected from ethyl acetate, dichloromethane, methyl ethyl ketone and methyl isobutyl ketone~~.

Claim 35. (Currently Amended) A method according to claim 1, wherein said active substance is a biologically active substance~~, which is preferably selected from proteins, (poly)peptides, (poly)nucleotides, plasmides and DNA~~.

Claim 36. (Currently Amended) A method according to claim 35, wherein said biologically active substance is selected from the group consisting of growth hormone, erythropoictin, interferon (α, β, γ-type), vaccine, epidermal growth hormone, Factor VIII, LHRH analogue, inulin, macrophage colony stimulating factor, granulocyte colony stimulating factor and interleukin.

E1 cont'd

Claim 37. (Currently Amended) A method according to claim 1, wherein said active substance is a biologically active substance in the form of a non-protein drug selected from the group consisting of ~~the following groups:~~ anti-tumor agents, antibiotics, anti-flammatory agents, antihistamines, sedatives, muscle relaxants, antiepileptic agents, antidepressants, antiallergic agents, bronchodilators, cardiotonics, antiarrythmic agents, vasodilators, antidiabetic agents, anticoagulants, hemostatics, narcotic agents and steroids.

Claim 38. (Currently Amended) A method according to claim 1, wherein said active substance is a non-biological substance~~, which is preferably selected from pesticide, fragrance, flavouring agent, catalyst and herbicide~~.

Claim 39. (Currently Amended) A method according to claim 1, wherein the amount of said active substance is in the range of about 0.001% to 90%~~, preferably about 0.01% to 70%, more preferably about 0.1 to 45%, and most preferably about 0.1 to 40%~~, said percentage being by weight based on the weight of the final particles.

Claim 40. (Currently Amended) A method according to claim 1, wherein the particles obtained in step c) are separated from said continuous phase~~, preferably by centrifugation or filtration followed by rinsing with water or other aqueous medium~~, and dried or allowed to dry, for instance in a vacuum, in the presence of a nitrogen gas flow, by lyophilisation or by air suspension drying.

Claim 41. (Previously Presented) A method according to claim 1, wherein step c) is performed such that the particles obtained are microspheres or capsules or nanospheres or capsules.

Claim 42. (Currently Amended) A method according to claim 41, wherein said particles have a mean diameter in the range of 10-200 μm~~, preferably 10-100 μm~~.

Claims 43-44. (Withdrawn)

Claim 45. (New) The method of claim 8, wherein the biodegradable polymer has a weight average molecular weight in the range of about 2000 to 110 000.

Claim 46. (New) The method of claim 10, wherein a copolymer of lactic acid/glycolic acid or a mixture of polylactic acid/polyglycolic acid is used as said biodegradable polymer, the weight ratio of (poly)lactic acid/(poly)glycolic acid being within the range of about 95/5 to 50/50.

E1 cont'd

Claim 47. (New) The method of claim 11, wherein the organic solvent is selected from the group consisting of ethyl acetate, dichloromethane, methyl ethyl ketone and methyl isobutyl ketone.

Claim 48. (New) The method of claim 12, wherein the active substance which is dispersed in step b) has a particle size within the range of about 0.5-10 μm.

Claim 49. (New) The method of claim 12, wherein the active substance which is dispersed in step b) has a particle size within the range of about 0.5-3 μm.

Claim 50. (New) The method of claim 13, wherein the active substance is a biologically active substance is selected from the group consisting of proteins, (poly)peptides, (poly)nucleotides, plasmids and DNA.

Claim 51. (New) The method of claim 16, wherein the active substance is a non-biological substance selected from the group consisting of pesticides, fragrances, flavouring agents, catalysts and herbicides.

Claim 52. (New) The method of claim 17, wherein the amount of said active substance is in the range of about 0.01% to 70%, said percentage being by weight based on the weight of the final particles.

E1 cont'd

Claim 53. (New) The method of claim 17, wherein the amount of said active substance is in the range of about 0.1 to 45%, said percentage being by weight based on the weight of the final particles.

Claim 54. (New) The method of claim 17, wherein the amount of said active substance is in the range of about 0.1 to 40%, said percentage being by weight based on the weight of the final particles.

Claim 55. (New) The method of claim 18, wherein the particles obtained in step c) are separated from said continuous phase by centrifugation or filtration followed by rinsing with water or other aqueous medium.

Claim 56. (New) The method of claim 25, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 20-60% (w/w).

Claim 57. (New) The method of claim 25, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 30-55% (w/w).

Claim 58. (New) The method of claim 25, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 30-50% (w/w).

E 1 cont'd

Claim 59. (New) The method of claim 26, wherein the polyethylene glycol has a molecular weight of about 5000 to 35000 Da.

Claim 60. (New) The method of claim 31, wherein wherein said biodegradable polymer has a weight average molecular weight in the range of about 2000 to 110,000.

Claim 61. (New) The method of claim 34, wherein said organic solvent used in step a) is selected from the group consisting of ethyl acetate, dichloromethane, methyl ethyl ketone and methyl isobutyl ketone.

Claim 62. (New) The method of claim 35, wherein the biologically active substance is selected from the group consisting of proteins, (poly)peptides, (poly)nucleotides, plasmids and DNA.

Claim 63. (New) The method of claim 38, wherein the non-biological substance is selected from the group consisting of pesticides, fragrances, flavouring agents, catalysts and herbicides.

Claim 64. (New) The method of claim 39, wherein the amount of said active substance is in the range of about 0.01% to 70%, said percentage being by weight based on the weight of the final particles.

E 1 cont'd

Claim 65. (New) The method of claim 39, wherein the amount of said active substance is in the range of about 0.1 to 45%, said percentage being by weight based on the weight of the final particles.

Claim 66. (New) The method of claim 39, wherein the amount of said active substance is in the range of about 0.1 to 40%, said percentage being by weight based on the weight of the final particles.

Claim 67. (New) The method of claim 40, wherein the particles obtained in step c) are separated from said continuous phase by centrifugation or filtration followed by rinsing with water or other aqueous medium.

Claim 68. (New) The method of claim 42, wherein wherein said particles have a mean diameter in the range of 10-100 μm.

Claim 69. (New) The method of claim 2, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 20-60% (w/w).

E 1 cont'd

Claim 70. (New) The method of claim 2, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 30-55% (w/w).

Claim 71. (New) The method of claim 2, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 30-50% (w/w).

Claim 72. (New) The method of claim 3, wherein the polyethylene glycol has a molecular weight of about 5000 to 35000 Da.

Claim 73. (New) The method of claim 1, wherein the homo- or copolymers prepared from α-hydroxy acids are lactic acid or glycolic acid or a combination thereof.

Claim 74. (New) The method of claim 1, wherein the homo- or copolymers prepared from cyclic dimers of α-hydroxy acids are lactides or glycolides or a combination thereof.

Claim 75. (New) The method of claim 24, wherein the homo- or copolymers prepared from α-hydroxy acids are lactic acid or glycolic acid or a combination thereof

Claim 76. (New) The method of claim 24, wherein the homo- or copolymers prepared from cyclic dimers of α-hydroxy acids are lactides or glycolides or a combination thereof.